

What is claimed is:

1. A synthetic antigen presenting cell (APC) for activating CD4⁺ T cells comprising:

a) a MHC class II α -chain gene operably linked to a first promoter in a vector capable of expressing a MHC class II α -chain;

b) a MHC class II β -chain gene operably linked to a second promoter in a vector capable of expressing a MHC class II β -chain, wherein upon expression of the α -chain and β -chain genes, the α -chain and β -chain form a MHC class II heterodimer capable of loading a peptide; and

c) at least one accessory molecule gene operably linked to a third promoter in a vector capable of expressing an accessory molecule, wherein at least one of the Class II genes and accessory molecule gene is lacking from the APC.

2. The APC of claim 1 wherein the α - and β -chain genes are of human origin.

3. The APC of claim 1 wherein at least one promoter is inducible.

4. The APC of claim 1 wherein the α -, β - and accessory molecule genes are present in the same vector.

5. The APC of claim 1 wherein at least one of the α -, β - and accessory molecule genes are present in a separate vector.

6. The APC of claim 1 wherein the APC is an insect cell.

7. The APC of claim 6 wherein the insect cell is selected from the group consisting of Spodoptera and Drosophila.

8. The APC of claim 1 further comprising a neomycin resistance gene operably linked to a vector.

9. The APC of claim 1 wherein the accessory molecule gene encodes a costimulatory molecule.

10. The APC of claim 9 wherein the costimulatory molecule is B7.1 or B7.2.

11. The APC of claim 1 wherein the accessory molecule gene encodes an adhesion molecule.
12. The APC of claim 11 wherein the adhesion molecule is ICAM-1, ICAM-2, ICAM-3, or LFA-3.
13. The APC of claim 1 wherein the accessory molecule gene encodes a survival molecule.
14. The APC of claim 13 wherein the survival molecule is Fas ligand or CD70.
15. The APC of claim 1 having a gene for a first accessory molecule and a gene for a second accessory molecule.
16. The APC of claim 15 wherein the first accessory molecule is a costimulatory molecule and the second accessory molecule is an adhesion molecule.
17. The APC of claim 16 wherein the costimulatory molecule is B7.1 or B7.2 and the adhesion molecule is ICAM-1.
18. The APC of claim 15 wherein the first accessory molecule is a costimulatory molecule and the second accessory molecule is a survival molecule.
19. The APC of claim 15 wherein the first accessory molecule is a survival molecule and the second accessory molecule is an adhesion molecule.
20. The APC of claim 19 wherein the survival molecule is CD70 and the adhesion molecule is ICAM-1.
21. The APC of claim 15 wherein the first and second accessory molecules are costimulatory molecules.
22. The APC of claim 21 wherein the costimulatory molecules are B7.1 and B7.2.
23. The APC of claim 1 having a gene for a first accessory molecule, a gene for a second accessory molecule and a gene for a third accessory molecule.
24. The APC of claim 23 wherein the first accessory molecule is a costimulatory molecule, the second accessory

molecule is an adhesion molecule, and the third accessory molecule is a survival molecule.

25. The APC of claim 24 wherein the costimulatory molecule is B7.2, the adhesion molecule is ICAM-1 and the survival molecule is CD70.

26. The APC of claim 1 wherein the MHC class II heterodimer and accessory molecule are present on the external surface of the APC in sufficient numbers for activating CD4⁺ T cells when a peptide is loaded onto the heterodimer.

27. The APC of claim 26 wherein the peptide is loaded extracellularly.

28. The APC of claim 26 wherein the peptide is loaded intracellularly.

29. The APC of claim 1 further comprising an antigen processing assisting gene operably linked to a fourth promoter in a vector capable of expressing an antigen processing assisting molecule.

30. A cell fragment derived from the APC of claim 1 having the MHC class II heterodimer and at least one accessory molecule operably associated on the fragment for activating CD4⁺ T cells.

31. The cell fragment of claim 30 wherein the MHC class II heterodimer is empty.

32. The cell fragment of claim 30 wherein a peptide is loaded onto the MHC class II heterodimer.

33. A synthetic antigen presenting matrix for activating CD4⁺ T cells comprising:

- a) a support;
- b) an extracellular portion of a MHC class II heterodimer operably linked to the support and capable of loading a selected peptide; and
- c) an extracellular portion of at least one accessory molecule operably linked to the support such that the

extracellular portions of the MHC class II heterodimer and accessory molecule are present on the matrix in sufficient numbers for activating CD4⁺ T cells when a peptide is loaded onto the extracellular portion of the heterodimer.

34. The matrix of claim 33 wherein the support is a cell fragment.

35. The matrix of claim 33 wherein the support is a cell.

36. The matrix of claim 35 wherein the extracellular portion of the MHC molecule is linked to the cell by a transmembrane domain of the MHC class II heterodimer.

37. The matrix of claim 33 wherein the support is a liposome.

38. The matrix of claim 33 wherein the support is a solid surface.

39. The matrix of claim 33 wherein the extracellular portion of the MHC class II heterodimer is linked to an epitope which reacts with an antibody to link the portion to the support.

40. The matrix of claim 33 wherein the extracellular portion of the Class II MHC heterodimer is linked to (His)₆ which reacts with nickel to link the portion to the support.

41. The matrix of claim 33 wherein the support is a porous material.

42. The matrix of claim 33 wherein the peptide is loaded onto the extracellular portion of the MHC class II heterodimer.

43. The matrix of claim 33 wherein the extracellular portion of the MHC class II heterodimer is empty.

44. The matrix of claim 33 wherein the accessory molecule is a costimulatory molecule.

45. The matrix of claim 44 wherein the costimulatory molecule is B7.1 or B7.2.

46. The matrix of claim 33 wherein the accessory molecule is an adhesion molecule.

47. The matrix of claim 46 wherein the adhesion molecule is ICAM-1, ICAM-2, ICAM-3 or LFA-3.

48. The matrix of claim 33 wherein the accessory molecule is a survival molecule.

49. The matrix of claim 48 wherein the survival molecule is Fas ligand or CD70.

50. The matrix of claim 33 having a first accessory molecule and a second accessory molecule.

51. The matrix of claim 50 wherein the first accessory molecule is a costimulatory molecule and the second accessory molecule is an adhesion molecule.

52. The matrix of claim 51 wherein the costimulatory molecule is B7.1 or B7.2 and the adhesion molecule is ICAM-1.

53. The matrix of claim 50 wherein the first accessory molecule is a costimulatory molecule and the second accessory molecule is a survival molecule.

54. The matrix of claim 50 wherein the first accessory molecule is a survival molecule and the second accessory molecule is an adhesion molecule.

55. The matrix of claim 54 wherein the survival molecule is CD70 and the adhesion molecule is ICAM-1.

56. The matrix of claim 50 wherein the first and second accessory molecules are costimulatory molecules.

57. The matrix of claim 56 wherein the costimulatory molecules are B7.1 and B7.2.

58. The matrix of claim 50 further comprising a third accessory molecule.

59. The matrix of claim 58 wherein the first accessory molecule is a costimulatory molecule, the second accessory molecule is an adhesion molecule, and the third accessory molecule is a survival molecule.

60. The matrix of claim 59 wherein the costimulatory molecule is B7.2, the adhesion molecule is ICAM-1 and the survival molecule is CD70.

61. A method of producing a synthetic antigen presenting cell (APC) comprising:

a) transforming a cell with an expressible MHC class II α -chain gene operably linked to a first promoter in a vector capable of expressing a MHC class II α -chain;

b) transforming a cell with an expressible MHC class II β -chain gene operably linked to a second promoter in a vector capable of expressing a MHC class II β -chain; and

c) transforming a cell with a first expressible accessory molecule gene operably linked to a third promoter in a vector capable of expressing an accessory molecule.

62. The method of claim 61 wherein the cell lacks a gene coding for at least one of the α -chain, the β -chain and the accessory molecule genes.

63. The method of claim 61 further comprising the step of transforming the cell with an expressible antigen processing assisting gene operably linked to a fourth promoter in a vector capable of expressing an antigen processing assisting molecule.

64. The method of claim 61 wherein the α - and β - chain genes are of human origin.

65. The method of claim 61 wherein at least one promoter is inducible.

66. The method of claim 61 wherein the α -, β - and accessory molecule genes are present in the same vector.

67. The method of claim 61 wherein the α -, β - and accessory molecule genes are present in separate vectors.

68. The method of claim 61 wherein the cell is an insect cell.

69. The method of claim 68 wherein the insect cell is selected from the group consisting of Spodoptera and Drosophila.

70. The method of claim 61 further comprising the step of transforming the cell with an expressible neomycin resistance gene operably linked to a vector.

71. The method of claim 61 wherein the accessory molecule gene encodes a costimulatory molecule.

72. The method of claim 71 wherein the costimulatory molecule is B7.1 or B7.2.

73. The method of claim 61 wherein the accessory molecule gene encodes an adhesion molecule.

74. The method of claim 73 wherein the adhesion molecule is ICAM-1, ICAM-2, ICAM-3 or LFA-3.

75. The method of claim 61 wherein the accessory molecule gene encodes a survival molecule.

76. The method of claim 75 wherein the survival molecule is Fas ligand or CD70.

77. The method of claim 61 further comprising the step of transforming the cell with a gene for a second accessory molecule.

78. The method of claim 77 wherein the first accessory molecule is a costimulatory molecule and the second accessory molecule is an adhesion molecule.

79. The method of claim 77 wherein the first accessory molecule is a costimulatory molecule and the second accessory molecule is an survival molecule.

80. The method of claim 77 wherein the first accessory molecule is a survival molecule and the second accessory molecule is an adhesion molecule.

81. The method of claim 77 further comprising the step of transforming the cell with a gene for a third accessory molecule.

82. The method of claim 81 wherein the first accessory molecule is a costimulatory molecule, the second accessory

molecule is an adhesion molecule, and the third accessory molecule is a survival molecule.

83. A method of producing a synthetic antigen presenting cell (APC) comprising:

a) providing a cell lacking a gene encoding at least one of MHC class II α -chain, MHC class II β -chain, and an accessory molecule; and

b) transforming the cell with an expressible gene for each of the genes of (a) lacking in the cell, the gene being operably linked to a promoter in a vector capable of expressing the gene.

84. A method of producing a synthetic antigen presenting cell (APC) comprising:

a) providing a cell lacking a gene encoding at least one of MHC class II α -chain, MHC class II β -chain, an accessory molecule and an antigen processing assisting molecule; and

b) transforming the cell with an expressible gene for each of the genes of (a) lacking in the cell, the gene being linked to a first operable promoter in a vector capable of expressing the gene.

85. A method of producing a synthetic antigen matrix comprising:

a) providing an extracellular portion of a recombinant MHC class II heterodimer;

b) providing an extracellular portion of at least one recombinant accessory molecule; and

c) linking the MHC class II heterodimer and accessory molecule to a support in sufficient numbers for activating CD4⁺ T cells when a peptide is loaded onto the MHC class II heterodimer.

86. The method of claim 85 wherein the accessory molecule is a costimulatory molecule.

87. The method of claim 86 wherein the costimulatory molecule is B7.1 or B7.2.

88. The method of claim 86 wherein the accessory molecule is an adhesion molecule.

89. The method of claim 88 wherein the adhesion molecule is ICAM-1, ICAM-2, ICAM-3 or LFA-3.

90. The method of claim 85 wherein the accessory molecule is a survival molecule.

91. The method of claim 90 wherein the survival molecule is Fas ligand or CD70.

92. A method for activating CD4⁺ T cells in vitro, the method comprising:

- a) providing the APC of claim 26;
- b) contacting the APC of step a) with CD4⁺ T cells, thereby inducing the contacted CD4⁺ T cells to proliferate and differentiate into activated CD4⁺ T cells.

93. The method of claim 92 further comprising:

- c) separating the activated CD4⁺ T cells from the APC.

94. The method of claim 93 further comprising the step of adding the activated CD4⁺ T cells to an acceptable carrier or excipient to form a suspension.

95. The method of claim 94 further comprising the step of administering the suspension to a patient.

96. A method for activating CD4⁺ T cells in vitro, the method comprising:

- a) providing the cell fragment of claim 30;
- b) loading the MHC class II heterodimer with a peptide; and
- c) contacting the peptide-loaded cell fragment with the CD4⁺ T cells, thereby inducing the contacted CD4⁺ T cells to proliferate and differentiate into activated CD4⁺ T cells.

97. The method of claim 96 further comprising the step of separating the activated CD4⁺ T cells from the cell fragment.

98. The method of claim 97 further comprising the step of adding the activated CD4⁺ T cells to an acceptable carrier or excipient to form a suspension.

99. The method of claim 98 further comprising the step of administering the suspension to a patient.

100. A method for activating CD4⁺ T cells in vitro, the method comprising:

- a) providing the matrix of claim 33;
- b) loading the MHC class II heterodimer with a peptide; and
- c) contacting the peptide-loaded cell matrix with the CD4⁺ T cells, thereby inducing the contacted CD4⁺ T cells to proliferate and differentiate into activated CD4⁺ T cells.

101. The method of claim 100 further comprising the step of separating the activated CD4⁺ T cells from the matrix.

102. The method of claim 101 further comprising the step of adding the activated CD4⁺ T cells to an acceptable carrier or excipient to form a suspension.

103. The method of claim 102 further comprising the step of administering the suspension to a patient.

104. A method for activating CD4⁺ T cells in vitro, the method comprising:

- a) contacting the APC of claim 1, the cell fragment of claim 30, or the matrix of claim 33, in an amount sufficient with a peptide library in vitro for a sufficient time to generate a peptide-loaded MHC class II heterodimer;
- b) contacting the peptide-loaded MHC class II heterodimer of step b) with CD4⁺ T cells, thereby inducing the contacted CD4⁺ T cells to proliferate and differentiate into activated CD4⁺ T cells.

105. A method of altering a CD4⁺ T cell-mediated immune response to treat a condition in a patient comprising:

- a) analyzing the patient for patient-specific cytokine profile;
- b) collecting CD4⁺ T cells from the patient;
- c) contacting the CD4⁺ T cells with the APC of claim 26 in vitro in a sufficient amount and for a sufficient time, thereby inducing the contacted CD4⁺ T cells to proliferate and differentiate into activated CD4⁺ T cells that produce a functionally opposing cytokine profile to the profile obtained in step a); and
- d) returning the activated CD4⁺ T-cells to the patient.

106. The method of claim 105 wherein the condition is an autoimmune disease.

107. The method of claim 106 wherein the autoimmune disease is selected from the group consisting of diabetes, multiple sclerosis, autoimmune thyroiditis, systemic lupus erythromatosus, mysasthenia gravis, Crohn's disease and inflammatory bowel disease.

108. The method of claim 106 wherein the patient-specific cytokine profile is produced by a CD4⁺ Th1 type response.

109. The method of claim 108 wherein the patient-specific cytokine profile comprises the cytokine selected from the group consisting of interleukin-2, interferon- γ and tumor necrosis factor.

110. The method of claim 105 wherein the condition is an allergy.

111. The method of claim 110 wherein the allergy is selected from the group consisting of asthma and contact sensitivity.

112. The method of claim 110 wherein the patient-specific cytokine profile is produced by a CD4⁺ Th2 type response.

113. The method of claim 112 wherein the patient-specific cytokine profile comprises the cytokine selected from the group consisting of interleukin-4 and interleukin-10.